At the outset, applicants wish to point out that independent claim 1 uses the transitional language "consisting essentially of". Thus, excluded from the compositions of claims 1 to 6 are any ingredients other than those specifically named, except where those additional ingredients would not materially affect the basic and novel characteristics of the claims.

It is respectfully submitted that the disclosure of Yanni cannot be the basis for a *prima facie* case of obviousness. The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. (MPEP § 2144.08, citing *In re Baird,* 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994)). The MPEP states that "it is essential that Office personnel find some motivation or suggestion to make the claimed invention in light of the prior art teaching. In the case of a prior art reference disclosing a genus, Office personnel should make findings as to:

(A) the structure of the disclosed prior art genus and that of any expressly described species or subgenus within the genus;

(B) any physical or chemical properties and utilities disclosed for the genus, as well as any suggested limitations on the usefulness of the genus, and any problems alleged to be addressed by the genus;

(C) the predictability of the technology; and

(D) the number of species encompassed by the genus taking into consideration all of the variables possible.

Yanni does not *specifically* disclose even one formulation. All of the Examples of Yanni require the inclusion of an active that must be chosen from one of the 10 neurokinin or bradykinin antagonists, set out at column 10, lines 24 to 42, which would place the compositions outside the scope of the compositions recited in claims 1 to 14. As acknowledged by the Examiner (bottom of page 4 of Office Action) all of the specific formulations of Yanni's Examples also contain disodium edetate (EDTA) which would also place the compositions outside the scope of the claims, as the "consisting essentially of" transitional language does not allow for the inclusion of EDTA, which is specifically disclosed in the present specification to protect ketotifen fumarate from decomposition under autoclaving conditions, i.e., would change a basic characteristic of the claimed compositions.

Yanni lists over 50 steroids, twelve growth factors, over 20 non-steroidal antiinflammatory drugs, five anti-oxidants, seven immunomodulators, ten antiallergics (including ketotifen), 18 antimicrobials, and the neurokinin and bradykinin antagonists mentioned above. Yanni states that any or all of these agents can be used, alone or in combination, to treat corneal haze (column 3, lines 17 to 26). The number of possible formulations that can be made with the agents listed by Yanni numbers in the millions. There is no disclosure or suggestion in Yanni pointing, out of all of the millions of possible formulations, to a formulation consisting essentially of ketotifen hydrogen

fumarate, glycerol, benzalkonium chloride, and water, much less in the specifically recited concentrations, as required by the present claims. As noted above, the only formulations that are more or less specifically suggested are those containing neurokinin or bradykinin antagonists, perhaps in combination with a steroid (see, e.g., claim 2 of Yanni), which is also excluded as an ingredient from the compositions recited in present claims 1 to 14. Accordingly, it is respectfully submitted that Yanni cannot properly be said to suggest the compositions or methods of the present claims, and the rejection of claims 1 to 14 over the disclosure of Yanni should be withdrawn.

The Examiner has also rejected claims 1 to 14 as obvious over the disclosure of Kurasawa et al. (JP 62 277323). Applicants respectfully traverse, and request reconsideration.

The Examiner has stated that "Kurasawa teaches an ophthalmic solution comprising ketotifen fumarate, benzalkonium chloride, glycerol, and water," citing to the Abstract of the Kurasawa application and the text. While the disclosure of Kurasawa might suggest a composition comprising ketotifen fumarate, glycerol, benzalkonium chloride, and water, it is respectfully submitted that Kurasawa cannot properly be said to disclose or suggest the compositions or methods of the claims, and most certainly does not encompass the compositions of the claims, i.e., compositions with a concentration of ketotifen hydrogen fumarate of 0.0345%. In fact, the disclosure of Kurasawa teaches away from making aqueous ophthalmic compositions comprising 0.0345% ketotifen hydrogen fumarate, as required by the present claims.

Applicants respectfully request that the Examiner reconsider the rejection of claims 1 to 14 in light of what Kurasawa teaches, *as a whole*. Kurasawa teaches ophthalmic solutions with a 0.1% concentration of ketotifen fumarate, approximately three times that recited in the present claims. Thus, Kurasawa teaches that a ketotifen fumarate-containing ophthalmic solution should have a concentration of 0.1% to be effective. Further, it is the express purpose of the Kurasawa invention to maintain the concentration of ketotifen fumarate as close to 0.1% as possible. It is very clearly taught that reducing the concentration of ketotifen fumarate below 0.1% is undesirable, and that this end (maintaining the concentration as close to 0.1% as possible) can be best achieved if a polyvalent alcohol or similar agent is used as a tonicity agent, as opposed to an electrolyte tonicity agent.

Thus, Kurasawa teaches away from decreasing the concentration of ketotifen fumarate in an ophthalmic solution below 0.1%, by providing methods to avoid such a decrease. There is certainly nothing in Kurasawa to indicate that a composition with the 0.0345% ketotifen concentration recited in the claims would be useful. When considered with Kurasawa's failure to suggest applicants' claimed specific concentration, it is respectfully submitted that one of ordinary skill in the art would actually have been deterred from even experimenting with ophthalmic compositions that contained

less than 0.1% ketotifen fumarate, much less the three fold lower concentration recited in the present claims.

Applicants submit that the Kurasawa reference being applied by the Examiner is similar to the "Wolf" reference applied by the Examiner in *In re Wiggins*, 397 F.2d 356 (CCPA 1968), submitted herewith. In *Wiggins*, the reference taught a composition comprising the active ingredient of the claimed compositions, but (as with the present claims) in a different dose, with no suggestion by the reference to modify the dose. Like Kurasawa, the Wolf reference had certain disclosures that would discourage those of ordinary skill in the art from experimenting with the dosage of active ingredient (in *Wiggins*, the claimed dose was higher than the disclosed doses). The CCPA found Wiggins's compositions to be not obvious over those disclosed by the cited Wolf reference. It is respectfully submitted that claims 1 to 14 are similarly not obvious in view of the disclosure of Kurasawa.

In light of the above remarks and the terminal disclaimer submitted herewith, it is respectfully submitted that the claims are in condition for allowance, and such action is earnestly solicited.

Respectfully submitted,

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